
Wnt proteins are self-renewal factors for mammary stem cells and promote their long-term expansion in culture.

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Public Summary:

Adult stem cells have the ability to self-renew and to generate specialized cells. Self-renewal is dependent on extrinsic niche factors but few of those signals have been identified. In addition, stem cells tend to differentiate in the absence of the proper signals and are therefore difficult to maintain in cell culture. The mammary gland provides an excellent system to study self-renewal signals, because the organ develops postnatally, arises from stem cells, and is readily generated from transplanted cells. We show here that adult mammary glands contain a Wnt-responsive cell population that is enriched for stem cells. In addition, stem cells mutant for the negative-feedback regulator Axin2 and therefore sensitized to Wnt signals have a competitive advantage in mammary gland reconstitution assays. In cell culture experiments, exposure to purified Wnt protein clonally expands mammary stem cells for many generations and maintains their ability to generate functional glands in transplantation assays. We conclude that Wnt proteins serve as rate-limiting self-renewal signals acting directly on mammary stem cells.

Scientific Abstract:

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